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# **IMPLANTS AND DEPOT INJECTIONS FOR TREATING OPIOID DEPENDENCE: QUALITATIVE STUDY OF PEOPLE WHO USE OR HAVE USED HEROIN**

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## **CONTRIBUTORS**

JS conceived of the study. JN and JS designed the study. CNET and RM conducted the focus groups. CNET and JN analysed the data. JN prepared the first draft of the paper and revised it following comments from JS, CNET and RM. All authors have approved the final article.

## **CONFLICT OF INTEREST**

JN receives honoraria and some expenses from *Addiction* journal in her role as Commissioning Editor and Senior Qualitative Editor. JS is a researcher and clinician who has worked with a range of types of treatment and rehabilitation service-providers. He has also worked with a range of governmental and non-governmental organizations, and with pharmaceutical companies to seek to identify new or improved treatments from whom he and his employer (King's College London) have received honoraria, travel costs and/or consultancy payments. This includes work with, during past 3 years, Martindale, Indivior, Mundipharma, Braeburn/Camurus and trial medication supply from iGen and from Camurus. His employer (King's College London) has registered intellectual property on a novel buccal naloxone formulation and he has also been named in a patent registration by a Pharma company regarding a concentrated nasal naloxone spray. For a fuller account, see JS's web-page at <http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx> RM has undertaken an unpaid student industry placement with Mundipharma Research Ltd. RM and JS have both worked as consultants for the United Nations Office on Drugs and Crime (UNODC). Subsequent to the submission of this article, JN, JS and CNET received a research grant from Camurus AB to undertake further qualitative research exploring long-acting buprenorphine.

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# **IMPLANTS AND DEPOT INJECTIONS FOR TREATING OPIOID DEPENDENCE: QUALITATIVE STUDY OF PEOPLE WHO USE OR HAVE USED HEROIN**

## **ABSTRACT**

### **Background**

Long-acting opioid pharmacotherapy (OPT) is presumed to offer benefits over more conventional OPT formulations. This paper analyses the views and experiences of people who use or have used heroin in order to explore two novel systems for delivering long-acting OPT: implants and depot injections. New materialism theorizing is used to interpret and frame the findings.

### **Methods**

Qualitative data were generated via 7 focus groups conducted during 2017 in London, UK. Participants (n=44; 28 men and 16 women; ages 33-66 years) had all received OPT. Focus group discussions covered real and potential OPT delivery systems. All participant data relating to implants and depot injections were coded using MAXQDA software and analysed inductively via Iterative Categorisation.

### **Findings**

Participants discussed implants and depot injections in terms of interacting physical, psychological and social factors: dose stability; OPT administration; stopping treatment; co-presence of an antagonist; breaking rituals and habits; reduced choice and control; feeling normal; information needs; getting on with everyday life; and social interaction. Participants identified both benefits and concerns, and variable needs and preferences, with respect to each delivery system.

### **Conclusions**

Implants and depot injections are not ‘fixed’ medications that can be administered to people to achieve pre-determined treatment aims. Rather, they are complex ‘assemblages’ with uncertain outcomes. Furthermore, they are themselves part of wider interactive ‘assemblages’. Drug developers and treatment providers need to understand this complexity in order to target long-acting OPT at people most likely to benefit from it, and to reduce any unintended negative consequences.

**KEYWORDS:** Qualitative study, opioid pharmacotherapy, opioid dependence, implants, depot injections, new materialism.

# **IMPLANTS AND DEPOT INJECTIONS FOR TREATING OPIOID DEPENDENCE: QUALITATIVE STUDY OF PEOPLE WHO USE OR HAVE USED HEROIN**

## **1. INTRODUCTION**

‘Opioid pharmacotherapy’ (OPT), ‘opioid substitution treatment’ (OST) and ‘opioid agonist treatment’ (OAT) are all terms that describe the administration of medications to people dependent on opioids in order to achieve ‘defined treatment aims’ (WHO/UNODC/UNAIDS, 2004). Pharmacotherapies for opioid dependence include opioid agonists (e.g. methadone), partial agonists (e.g. buprenorphine), opioid antagonists (e.g. naltrexone), and  $\alpha$ -2-adrenergic agonists (e.g. lofexidine) (Stotts et al., 2010). Traditionally, pharmacotherapy has tended to be taken daily, in liquid or tablet form, and under close medical supervision. More recently, long-acting formulations have become available for clinical practice. For example, the United States Food and Drug Administration (FDA) approved the first buprenorphine implant (6-month duration) in May 2016 and a first buprenorphine depot injection (monthly administration) in November 2017 (Sigmon and Bigelow, 2016). Other products, such as naltrexone implants, have been developed and the market is expanding (Comer et al., 2007; Hegde et al., 2013; Stotts et al., 2010).

Long-acting OPT is presumed to offer benefits over more conventional OPT formulations. By providing sustained medication release, it makes daily dosing unnecessary, so reducing the frequency of clinic/pharmacy visits and obviating the need for take-home doses. This is expected to improve patient adherence, reduce the treatment burden (for both patients and clinicians), and remove the risk of illicit diversion (Sigmon et al., 2006; Sigmon and Bigelow, 2016). These claims have not, however, been tested to-date. Typically, studies of new medicinal products are conducted by natural scientists who assume that medicines have inherent physical properties, which cause predictable changes in patients once administered (Bundy and Quintero, 2017; Gomart, 2002). Their research, conducted primarily for drug development and regulatory purposes, focuses on product characterization, safety and efficacy (such as dose, storage requirements, side effects, adverse reactions, pharmacokinetics, and metabolism) (DiMasi, 2002; Gad, 2017; Rosenthal et al., 2013).

Social scientists have, meanwhile, argued that medicines and their effects relate to complex social and cultural factors that vary across time and place (Gomart, 2002; Barad, 2007). Working largely within a social constructivist paradigm, social scientists began to study OPT during the 1990s. Their initial research was descriptive and applied, exploring heroin users’ views and experiences of methadone, and their reasons and motivations for engaging with methadone treatment (Jones et al., 1994; Koester et al., 1999; Murphy and Irwin, 1992; Neale, 1998, 1999a, 1999b; Sheridan and Barber, 1996). Later, studies became more

theoretical, drawing upon sociological and psychological concepts such as identity, stigma, surveillance, and social control (see, for example, Harris and Rhodes, 2013; Monaghan and Wincup, 2013; Radcliffe and Parkes, 2013; Strike et al., 2013; Treloar and valentine, 2013).

In recent years, social scientists have also drawn upon the interdisciplinary field of ‘new materialism’ to understand methadone and methadone treatment (Fraser and valentine, 2008; Gomart, 2002; Keane, 2013; valentine, 2007). New materialism is distinct from biological and constructivist approaches to understanding the world in that the physical/natural and the social/cultural are considered contiguous rather than distinct. The focus of new materialism is on ‘matter’; a generic term used to encompass physical and material things, but also human bodies, other animate organisms, and more abstract concepts such as places, spaces, time, and practices (Braidotti, 2013; Fox, 2016; Fox and Alldred, 2018; Haraway, 1991). Proponents of new materialism maintain that all matter – that is, all human and non-human phenomena – is relational and contingent rather than fixed or stable (Barad, 1996; Coole and Frost, 2010; Fox, 2016). Matter affects and is affected by other matter, and all matter is produced in interacting networks (or ‘assemblages’) of other matter (Deleuze and Guattari, 1988).

Drawing upon new materialism, and particularly actor-network theory (a key strand of new materialism), Gomart (2002), valentine (2007) and Fraser and valentine (2008) have all argued that methadone, being matter, is neither a stable, pre-existing chemical substance nor a social construction. Methadone is simultaneously a physical phenomenon with biochemical properties *and* a deeply social, cultural and political phenomenon. It is multivalent, linked to other matter, relational and interactive. Methadone varies from one context to another. It acts pharmacologically (producing tangible physiological effects) but only in interaction with other human and non-human ‘actants’ (Bundy and Quintero, 2017). In short, methadone’s qualities are not inherent in its pharmaceutical properties, but are co-produced within complex networks of other matter (Bundy and Quintero, 2017; Latour, 2005; Law, 1999).

In this paper, our focus is neither on methadone nor on any other specific medication. Our aim is rather to explore two novel systems for delivering long-acting OPT (implants and depot injections), and we do this from the perspective of people who use or have used heroin. Our interest follows from the argument that OPT is likely to be more effective if we take patients’ views, experiences and motivations into account when making treatment decisions (Neale, 1999a; Neale, 2013). In the Discussion, we return to new materialism to help interpret and frame our findings.

## 2. METHODS

Data were generated as part of a qualitative focus group (FG) study exploring real and imagined OPT delivery systems: liquids, tablets, nasal sprays, implants and depot injections. Qualitative methods are frequently used to investigate the acceptability of emergent health care interventions, including new medicines. This kind of inquiry can be undertaken using interviews or focus groups conducted with people who have not received the intervention

under investigation, but who belong to the target patient population or to a closely related population. For example, a number of published studies have explored women's hypothesized perceptions of permanent and long-acting contraception, including implants and depot injections (Glasier et al., 2008; Harrington et al., 2015; Zimmerman et al., 1990).

In this study, the participants (n=44) were all current or former heroin users (28 men and 16 women; ages 33-66 years). The groups were conducted in drug and alcohol services, a peer support recovery service, and a homeless hostel in London, UK, during March and April 2017. Ethical approval for the study was granted by the United Kingdom (UK) NHS Research Ethics Service. Recruitment of participants occurred in several ways: posters with the researchers' contact details were displayed in the services; researchers approached potential participants in person at the services; workers encouraged service users to contact the researchers; and participants from the earlier focus groups introduced the study to their peers. Everyone who expressed interest in taking part (n=76) completed a basic screening questionnaire that covered gender, age, ethnicity, substance use, prescribed medications, and contact details. The researchers then used the screening information to identify and invite people to the groups.

Groups were organised according to participants' current treatment status to minimise the likelihood of anyone comparing their own treatment with other treatments and then becoming dissatisfied. This resulted in 7 groups: oral methadone (FGs 1 and 2); buprenorphine tablets (FGs 3 and 4); injectable OPT (FG5); and former OPT (FGs 6 and 7). Participants in FG6 reported no current opioid use at all whereas participants in FG7 were all current users of street opioids. One participant had previously participated in a trial of depot injection buprenorphine and several others knew people who had had naltrexone implants. In addition, one female participant reported that she had had a contraceptive implant. Others were familiar with the concept of receiving contraception or treatment for mental health problems via depot injections (see Table 1 for additional participant details).

TABLE 1

Each group was facilitated by two researchers who used a topic guide to structure the discussions. The guide initially focused on participants' personal experiences of OPT before exploring their views of receiving treatment for opioid dependence via the different delivery systems. No specific medications were mentioned as the objective was to focus attention on 'how' the treatment was delivered rather than the particular drug. Participants were provided with a brief verbal description of each delivery system and then asked what they thought about it, including what they liked and disliked. The information provided to participants about implants and depot injections is shown in Table 2.

TABLE 2

Groups lasted between 41 and 63 minutes and were audio recorded. All participants received £10 as a gesture of thanks. Audio recordings were transcribed verbatim and then coded using

the qualitative software MAXQDA (version 11). The coding frame comprised deductive codes derived from the topic guide and inductive codes emerging from the data. For this paper, all coded data relating to implants and depot injections were exported from MAXQDA into Microsoft Word documents and then analysed inductively through a process of Iterative Categorisation (Neale, 2016).

In the first stage of the analyses, the coded implant and depot injection data were reviewed line by line to describe aspects of each delivery system that participants liked and disliked. Since similar issues were discussed in relation to both systems, and positive comments were often opposites of the negative comments, the analyses were merged and then grouped into more inductive categories. These categories (n=10) were subsequently organised under three headings: i. physical factors (4 categories); ii. psychological factors (4 categories); and iii. social factors (2 categories). We use these categories to structure the findings below. Differences between participants' views of the implants and depot injections, and any emergent differences between sub-groups of people receiving OPT, were considered and documented as part of the analytical process.

### **3. FINDINGS**

#### **3.1. Physical factors**

##### **3.1.1. Dose stability**

Many participants liked the idea that implants and depot injections guaranteed a regular dose of OPT every day. They argued that this was '*straightforward*' and would help them to feel '*stable*' and '*on a level*'. Moreover, it would offer welcome protection from a range of contingencies, such as missed doses (e.g. if someone was unable to attend the pharmacy to collect their medication), lost doses (e.g. if someone accidentally spilt medication) and presumed harms associated with other OPT formulations (e.g. tooth decay linked to the sugar in oral methadone):

“Makes sense to me as it [long-acting OPT] is easy, straightforward. You know where you are.” (FG2, male)

In contrast, other participants disliked the concept of a stable daily dose. Some expressed concern, particularly in respect of the implant, that they would be '*stuck*' on the same dose of OPT and not able to increase or reduce it as they wanted. Others stated that they were used to taking substances (street drugs or OPT) every day in order to feel '*different*', '*human*', or '*alive*'. Therefore, they did not want to feel '*flat*' or '*not stoned*' as this would likely be '*boring*':



“I don’t like the sound of that [depot injection] because it means that you’re on a level for the whole month... I used to like getting up in the mornings and taking my methadone, knowing that in half an hour I’m going to have that really warm glow inside.” (FG6, male)

### **3.1.2. OPT administration**

Participants regularly voiced concerns about the process of fitting the implants and to a lesser extent the injection of the depot formulation. Worries about the implant included the intrusive nature of the surgical insertion process, needing to have multiple implants inserted over time which might cause scarring (*‘we’ll look like Frankenstein’*), and potential for infection:

“You’d be going for surgery, minor surgery, every time you went. I’d be worried about infection.” (FG5, female)

Additionally, participants were often apprehensive about having something *‘invasive’* that they did not *‘trust’*, *‘a little bot’*, *‘nanite’* or *‘microchip’* implanted inside them. In terms of the depot injection, participants explained that they were worried that the injection would be painful or might create a haematoma or that the procedure would be a negative reminder of an injecting history that they were trying to forget. Some also said that they disliked or feared needles:

“I wouldn’t even go there, not even think about it [depot injection], because I don’t like needles.” (FG7, male)

### **3.1.3. Stopping treatment**

For many participants, a major disadvantage of the depot injection was that it could not be removed from the body once administered: *‘once it’s in, it’s in’*. As already reported, some participants did not like the idea of being unable to change the dose until it depleted. Others feared what might happen to them if they experienced side effects or allergic reactions after the medication had been injected. In addition, some worried that depot injections would put people at increased risk of opioid overdose or might prevent people from receiving effective pain relief should they be involved in an accident:

“You would want to know at the end of the day that you could remove it [depot injection]. For instance, if... you had a bad reaction to it.” (FG4, male)

Overall, participants felt that an OPT implant was preferable to a depot injection in terms of stopping treatment since the implant could be removed by a professional. Moreover, they could even take it out themselves if they were unhappy or had an adverse reaction.

Evidencing this, participants spoke of knowing people who had ‘*cut out*’ naltrexone implants with a scalpel or razor blade (‘*hacking themselves up*’) because they had wanted to use street drugs:

“If I suddenly wanted it [implant] out and I was in an irrational state, I’m not going to have the wherewithal to think ‘Oh, I’ll wait until the morning... get the proper doctor to do it’.” (FG5, male)

Despite this, participants still voiced concerns that the implant might not be easy to take out, particularly if it had ‘*moved*’, ‘*got stuck*’, or become ‘*difficult to locate*’.

#### **3.1.4. *Co-presence of an antagonist***

In assessing long-acting OPT, participants routinely reported that it was important to know whether or not the medication contained an antagonist drug to ‘*block*’ the effects of street opioids. Nonetheless, opinions were divided on what was best. Some emphasized that the antagonist was beneficial as it would enable them to stop thinking about substances and so not use street drugs:

“If it [OPT with antagonist] is going to give me three months away from street drugs, then of course I’m going to embrace it.” (FG3, male)

Indeed, according to some, there was no point in having long-acting OPT if it did not contain antagonist medication. These participants tended to be those most motivated to achieve abstinence. Others, meanwhile, disliked the idea that a ‘*blocker*’ might be included in the formulation, expressing concern that they would *not* be able to use street opioids on top of the medication. Furthermore, they might overdose if they tried.

### **3.2. Psychological factors**

#### **3.2.1. *Breaking rituals and habits***

Many participants reported that an important benefit of long-acting OPT (both implants and depot injections) was their potential to help people break negative rituals and habits relating to collecting and taking daily medications. Participants often observed that daily routines relating to prescription drugs were effectively extensions of using street drugs. Moreover, they undermined treatment progress by ‘*tying them down*’:

“A lot of the things that go along with getting a script... are habit-forming in themselves. Not just drinking the juice [methadone]. Getting the juice... waking up

not feeling human until you do that ritual of drinking... they [daily routines] tie you down.” (FG2, female)

According to some participants, not having to take medication daily would be particularly valuable for people just starting OPT, since it would prevent them from developing habit-forming behaviours around treatment in the first place. Others felt that those nearing the end of treatment would benefit as long-acting formulations could help to wean them off any rituals already established. Notably, however, one participant stated that he did not like the idea of implants or depot injections precisely because he would miss the daily rituals of taking medication:

“I go to the chemist and I get home, have me tea, have me juice [methadone], and I feel it kick in as it were... And I’m so used to that.” (FG2, male)

### **3.2.2. *Reduced choice and control***

Frequently, participants complained that long-acting OPT (both implants and depot injections) would reduce the amount of choice and control they would have over their medication and lives more generally. Not being able to change or manage their dosage caused many to worry that they would feel ‘*powerless*’, that they would lose some of their autonomy, and that they would be less responsible for themselves. In short, they would become a ‘*hostage*’ to their medication and the implants and depot injections would be ‘*in control of them*’:

“I want to be in control, not some substance under my skin.” (FG4, male)

Participants who were receiving take-home or injectable OPT were especially worried about this aspect of long-acting formulations, explaining that they were accustomed to managing their own medication by taking it as and when they wanted or needed during the day. Despite this, some participants suggested that removing control could be an advantage in respect of people who might be tempted to use street opioids.

### **3.2.3. *Feeling normal***

Across all the focus groups, a frequently reported perceived benefit of both implants and depot injections was their ability to help people feel ‘*normal*’:

“That’s when you will be normal. That is normality. Do you get what I mean? It’s like you’re not even a drug addict anymore.” (FG1, female)

Participants gave several interconnected reasons for this. First, implants and depot injections were invisible, so nobody would know they were receiving OPT. Second, long-acting

formulations removed the constant need to attend drug services, doctor surgeries and pharmacies; activities that were in themselves disruptive of feeling ‘*normal*’, not least as participants felt they were always making excuses to hide their disappearances. Third, participants stated that having an implant or depot injection would mean that pharmacists would no longer be able to treat them ‘*differently*’ or like ‘*an addict*’. Women, in particular, liked the fact that long-acting formulations were discreet and invisible to other customers in the pharmacy and to the outside world in general:

“I think there’s less stigma attached to something that nobody can see. You don’t drink it, you don’t take it, you’re just another person, and nobody has to know that you’ve got that [implant] under your skin.” (FG2, female)

### **3.2.4. Information needs**

Although participants were often familiar with implants and depot injections for contraception or mental health problems, they still reported that long-acting formulations were a new concept for those receiving OPT. Consequently, their knowledge was often limited:

“It’s very novel, especially for people that are drug users... I suppose it’s a new thing that people aren’t aware of.” (FG6, male)

Participants had many questions and expressed interest in learning more. For example, they wanted to know how the technology worked; whether or not it was reliable; what the likely side-effects were; whether it might induce withdrawal symptoms; how they would feel as the medication wore down; how long opioids would remain in their body; whether implants would dissolve or melt; how implants were removed; whether there would be interactions with other medications; how they might receive pain relief if needed; whether they would be able to drive a car; what the implications were for overdosing on street drugs; whether they could vary the dose; whether the dose could be reversed; and how they would wean themselves off treatment. Importantly, the absence of such information generated scepticism but also fear:

“Lots of medications interact with each other. So what happens if you get unwell and you’re in a hospital and it’s already in you, and you might need some medication that interacts with it? It just seems really toxic and scary for me.” (FG6, female)

## **3.3. Social factors**

### **3.3.1. Getting on with everyday life**

According to many participants, having to attend appointments or travel to pharmacies to collect their OPT was so burdensome and stressful that it hindered their efforts to ‘*get on with life*’. For example, one man reported that he never visited his family who lived in another city as he would be too ‘*scared*’ about not being able to get his daily buprenorphine prescription whilst away. Reflecting this, many participants – particularly those who had been attending pharmacies for daily supervised consumption for many years and those wanting to reduce or come off their OPT – argued that long-acting OPT had another major benefit. By reducing the need to attend services all the time, it would ‘*free*’ them to do more ‘*constructive things*’:

“You know it’s there [depot injection]. It’s good, it’s brilliant, because you can get on with your life and stuff. It frees you up.” (FG2, male)

In particular, participants welcomed the fact that long-acting OPT would enable them to carry out daily chores, fulfil parenting duties, travel, go on holiday, spend time with family, attend college, and secure paid employment:

“You could go to work, yeah, all that stuff... You could go to work, go to college, whatever.” (FG3, female)

### **3.3.2. *Loss of social interaction***

As already documented, many participants emphasized that not having to attend pharmacies and services regularly was an important benefit of long-acting OPT. Nonetheless, some – mostly those who had more recently started treatment and those who also reported mental health problems – stated that they would miss attending services. This was because treatment-related appointments gave them a reason and motivation to go out and interact with other people. In other words, standard OPT offered somewhere to go and something to do. For example, one woman who had a diagnosis of bipolar disorder said that she liked going to the pharmacy as the journey provided her with structure, daily exercise, and a reason to leave the house:

“I like going to the chemist every day... It gets me out the house... I’m bipolar. So if I don’t have to go out, I’ll just stay indoors in my pyjamas.” (FG3, female)

Another male participant, who reported depression, explained that the only time he left home was to go to the pharmacy and he looked forward to this each morning as it was his only social interaction:

“Going to the chemist on a daily basis actually gets me outside the house. Because I don’t go outside, I really don’t do anything. I’m clinically depressed... That would be it, 24 hours a day inside. I wouldn’t be going out and talking to anyone.” (FG2, male)

#### 4. DISCUSSION

Our research has explored implants and depot injections for treating opioid dependence from the perspective of people who use or have used heroin. This has helped us to understand how these new delivery systems will likely be received by patients as they become more widely available for OPT. Participants agreed that both delivery systems offered benefits. For example, they were discrete and could therefore reduce the stigma that people often experience as OPT clients (particularly when collecting medication from pharmacy services). Not having to constantly attend services and appointments could also free patients to pursue other activities and begin to live ‘normal’ lives (c.f. Nettleton et al., 2013).

Despite these benefits, participants worried about the fitting of the implants, the injecting of the depot formulations, having foreign matter inside them, and being unable to control the medication dose or stop treatment once started. Participants also often disagreed about particular features of long-acting OPT. Thus, some welcomed having a stable daily dose or less contact with treatment services whereas others emphasized that they would miss the variable sensations associated with oral methadone’s shorter duration of action or would be socially isolated if they did not have their daily trip to the pharmacy.

Participants’ accounts illustrated how needs, preferences and perceptions of long-acting OPT varied depending on patient characteristics and circumstances, including gender, comorbidity, and whether or not someone was new to treatment or motivated to achieve abstinence (see also Hatcher et al., 2018). These findings are consistent with the social science literature on OPT, and particularly Fraser and valentine’s observation that methadone is multivalent (Fraser and valentine, 2008). Long-acting OPT delivered by implants and depot injections are similarly not ‘fixed’ medications that can be administered to achieve pre-determined treatment aims (WHO/UNODC/UNAIDS, 2004). They are complex webs of physical, psychological and social factors with uncertain outcomes.

Long-acting OPT can thus be usefully considered as an ‘assemblage’. It may comprise an implant or depot injection, but also a dose, with a particular duration of action, with or without an antagonist. Moreover, it is fitted in a certain way, is manufactured to disperse medication in a particular manner, and might function reliably or not. Additionally, implants and depot injections are themselves part of wider ‘assemblages’. Accordingly, they might be contraindicated by other medications, they are understood via information sources (or lack of them), and they are judged by their interactions with ability to drive, risk of overdose, feelings of control, daily rituals and habits, patient/ professional interactions, wider social and familial relationships, ability to travel, and employment opportunities etc.

Participants in our study clearly recognized the capacity of long-acting OPT to ‘act’. On the one hand, implants and depot injections could invade, hurt or infect their bodies, move around or ‘get stuck’, induce memories of an injecting past, control them, and generate fear. On the other, they had the potential to help people break rituals and habits, feel ‘normal’, and

‘*get on with life*’. Importantly, however, our participants did not presume that implants and depot injections were fixed or immutable phenomena. Consistent with the principles of new materialism, these new delivery systems were variable entities that could be affected by other matter. Most obviously, long-acting OPT could be countered by the consumption of street drugs, implants could be removed under medical supervision or by patients themselves, and concerns about toxicity and safety might be mitigated by better information.

#### **4.1. Limitations and strengths**

Our findings are subject to the same limitations as any qualitative study, including small sample size and consequent poor empirical generalizability (Neale et al., 2005; Neale et al., 2013). In addition, our findings could have been categorized and presented under different headings given the overlap between the issues discussed. Despite this, our study is the first in-depth qualitative exploration of implant and depot formulations of OPT from the perspective of people who use or have used heroin. Our sampling was inclusive of current and former heroin users and a range of treatment (and out-of-treatment) groups. We additionally established parallels with previous empirical and theoretical work on other OPT formulations, particularly methadone. Taken together, this provides support for the transferability of our findings to other contexts and settings (Lincoln and Guba, 1985).

### **5. CONCLUSIONS**

New OPT formulations as delivered by implants and depot injections seem no more likely to be silver bullets for opioid dependence than methadone (Paxton et al., 1978). Moreover, the need for qualitative research that provides insights into the views, experiences and motivations of those for whom OPT is intended remains as important now as it ever was. We suggest that patients will view and engage with implants and depot injections in complex ways depending on interacting physical, psychological and social factors. Both drug developers and treatment providers need to understand this complexity in order to increase the likelihood that long-acting OPT is targeted at people most likely to benefit from it, but also to reduce the risk of unintended negative consequences (e.g. self-removal of implants, patients feeling disempowered, premature loss of contact with professionals, and overdose).

To conclude, we suggest that developers of implants and depot injections should actively seek to build flexibility and choice into their products, particularly in relation to dosage, duration of action and partial agonist/antagonist combinations. Given heroin users’ concerns about the irreversibility of long-acting OPT, options for smaller dosages and shorter durations of action that can be increased incrementally could be beneficial. Crucially, there also seems to be a need for accessible information to help potential patients understand, and make informed decisions about, these new products. The content and format of this information could be developed with heroin users to ensure that it addresses their questions and uses appropriate media and language. Prescribers similarly need to provide potential patients with

verbal information, and afford them sufficient opportunity to ask questions and discuss concerns before commencing any long-acting treatment. Since some heroin users are likely to be anxious about losing the professional contact associated with daily dosing, the need for - and availability of – replacement psycho-social support should likewise be carefully considered.



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**Table 1: Participant details**

Demographic characteristics	FG <sup>a</sup> 1 Oral methadone (n=4)	FG2 Oral methadone (n=8)	FG3 Buprenorphine tablets (n=8)	FG4 Buprenorphine tablets (n=8)	FG5 Injectable OPT <sup>b</sup> (n=6)	FG6 Former OPT: no current street opioids (n=6)	FG7 Former OPT: current street opioid use (n=4)	All (n=44)
<b>Gender</b>								
Male	2 (50%)	5 (63%)	6 (75%)	5 (63%)	4 (67%)	4 (67%)	2 (50%)	28 (64%)
Female	2 (50%)	3 (38%)	2 (25%)	3 (38%)	2 (33%)	2 (33%)	2 (50%)	16 (36%)
<b>Ethnicity</b>								
White /White British <sup>c</sup>	2	4	6	6	5	4	2	29 (66%)
Asian /Asian British	0	0	0	0	0	0	0	0 (0%)
Black /Black British	2	2	1	0	0	2	1	8 (18%)
Mixed or Multiple	0	1	1	1	0	0	0	3 (8%)
Other	0	1	0	1	1	0	1	4 (8%)
<b>Age</b>								
Mean age (years) (range)	49 (42-59)	51 (43-58)	46 (33-55)	40 (34-47)	56 (47-66)	47 (39-58)	45 (35-53)	48 (33-66)
<b>Street opioid use</b>								
Mean age of first use (range)	23 (16-33)	18 (14-22)	24 (14-31)	23 (14-35)	18 (15-27)	22 (15-32)	23 (18-26)	22 (14-35)
Mean duration of use (range)	26 (22-30)	33 (25-39)	22 (2-37)	17 (0-33)	39 (27-50)	n/a	22 (9-31)	26 (0-50)
Current street opioid use	4 (100%)	6 (75%)	4 (50%)	2 (25%)	2 (33%)	n/a	4 (100%)	22 (53%)
<b>Current treatment<sup>d</sup></b>								
None	0	0	0	0	0	6	4	10 (23%)
Buprenorphine (tablets)	0	0	8	8	0	0	0	16 (36%)
Methadone (oral)	4	8	0	0	2	0	0	14 (32%)
Methadone (injection)	0	0	0	0	2	0	0	2 (5%)
Diamorphine (injection)	0	0	0	0	4	0	0	4 (9%)

<sup>a</sup> Focus group; <sup>b</sup> Opioid agonist treatment; <sup>c</sup> 21 participants identified as 'British', 4 as 'Italian', 3 as 'Irish', and 1 as 'European'; <sup>d</sup> 2 participants were prescribed a combination of opioid medications (injectable + oral). The denominator used for the calculation of percentages across all subjects was n=44. Because two subjects from FG5 were included in the percentages for 'Current treatment' twice, the total percentage across all 44 subjects adds up to 105%.

**Table 2: Information provided to participants about implants and depot injections**

- **AN IMPLANT** is a pellet which gets inserted under the skin. Following a local anesthetic, a small cut is made to the skin, and the implant is slipped into the tissue under the skin. Once in place, it slowly releases the medication over the course of several months.
- **A DEPOT INJECTION** is given by a doctor or a nurse, usually into the muscle. The injection slowly releases the medication which potentially lasts a month or two.